consequently reduce chances of survival. Models to predict acute dysphagia are available. However, these models were based on limited amounts of data and the performance of these models needs improvements before implementation into routine practice. Furthermore, Bayesian network models are shown to perform better than conventional modeling techniques on datasets with missing values, which is a common problem in routine clinical care. In this work, we train a Bayesian network model on a large clinical datasets, originating predominantly from routine clinical care, to accurately predict acute dysphagia in NSCLC patients during and shortly after (C)RT.

Material and Methods: Clinical data from 1250 inoperable NSCLC patients, treated with radical CRT, sequential chemo-radiation or RT alone were collected. The esophagus was delineated using the external esophageal contour from the cricoid cartilage to the GE junction. A Bayesian network model was developed to predict severe acute dysphagia (Grade 3 according to the CTCAEv3.0 or v4.0). The model utilized age, mean esophageal dose, timing of chemotherapy and N-stage to make predictions. Variable selection and structure learning was done using the PC-algorithm. The model was trained on data from 1250 patients. The model's performance was assessed internally and on an external validation set (N=218) from the United Kingdom. Model discriminative performance was expressed as the Area Under the Curve (AUC) of the Receiver Operating Characteristic (ROC). ROCs were compared using the method proposed by DeLong and colleagues. Model performance was also assessed in terms of calibration. Calibration refers to the agreement between the observed frequencies and the predicted probabilities and is expressed as the coefficient of determination (r2).

Results: One-hundred forty patients (11,2%) developed acute dysphagia (≥ Grade 3 according to the CTCAEv3.0 or v4.0). The model was first validated internally, by validating on the training cohort (N=1250, AUC = 0.77, 95% CI: 0.7325-0.8086, r2 = 0.99). Subsequently, the model was externally validated on a UK dataset (N = 218, AUC = 0.81, 95% CI: 0.74-0.88, r2 = 0.64). The ROC curves were not significantly different (p = 0.28).

Conclusion: The Bayesian network model can make accurate predictions of acute dysphagia (AUC = 0.77, 0.81 in the internal and external validation respectively), making it a powerful tool for clinical decision support.

OC-0258

Linear-quadratic modeling of acute rectum toxicity in a prostate hypo-fractionation trial

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Purpose or Objective: In the Dutch prostate hypo-fractionation trial (19x3.4Gy versus 39x2Gy) a higher incidence of acute gastro-intestinal toxicity was observed in the experimental arm. We performed model estimations using various alpha/beta ratios to determine whether this difference can be explained according to the linear-quadratic model.

Material and Methods: Patients with localized prostate cancer were randomized between standard fractionation (SF=5x2Gy per week, N=293) and hypo-fractionation (HF=3x3.4Gy per week, N=285). Proctitis (grade 2+) was defined as moderate to severe mucous or blood loss, or mild mucous or blood loss combined with at least 2 other complaints: diarrhea, incontinence, tenesmus, cramps, pain. Peak incidences over treatment weeks 4 and 6 were available from prospectively collected patient reports. Normalized Total Dose (NTD, 2Gy equivalent) was accumulated per week for alpha/beta ratios of 3, 5, 10, and∞ (=physical dose), and used to derive relative Dose-Surface Histograms (DSHs) of the delineated anorectum for each patient. Maximum likelihood logistic regressions were performed using a DSH point as variable. Univariate (UV) models and multivariate (MV) models with fractionation schedule as factor were constructed.

Results: Acute proctitis incidences were highest for hypo-fractionation (SF: n=67; 22.9%, HF: n=98; 34.3%, p<0.01). The 7Gy/week DSH point correlated well with proctitis, and was used for subsequent modeling. Figure 1 illustrates the models for the various alpha/beta ratios, and incidences for five (roughly) equal size patient bins. Note that the NTD correction decreases the surface areas that receive <2Gy per day, and increases surfaces receiving >2Gy. The central NTD values of the patient bins therefore lie at higher values for HF than for SF. The MV models have higher likelihood than the UV models, but likelihood for different alpha/beta ratios is similar. All MV models have odds ratios >1.5 (p<0.05) for HF versus SF, i.e. fractionation remains a factor.

Conclusion: Linear-quadratic dose correction cannot explain the observed acute rectum toxicity difference between hypo-fractionated and standard treatment in patients with prostate cancer. Subsequent modeling will concentrate on alternative mechanisms.

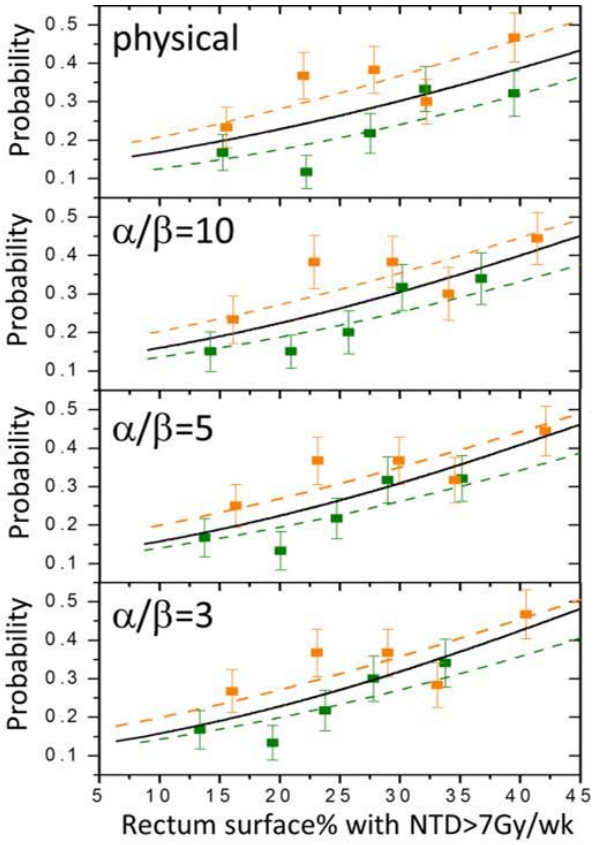

Figure 1 Acute proctitis models (UV solid, MV dashed) for standard (green) and hypo-fractionation (orange)

OC-0259

Spatial rectal dose-response for patient-reported leakage, obstruction, and urgency in prostate RT

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